

**REMARKS****Disposition of Claims**

Claims 1-62 were pending in the present application. Claims 1-21, 31-59, and 62 were withdrawn from consideration. By virtue of this response, claims 22, 29-30, 33-34, 40-45, 51-52, 54-55, and 61-62 have been amended, claims 23-27, 32, 53, 56, and 59-60 have been cancelled and new claims 63-73 added. Support for the amended and new claims can be found throughout the specification, including the claims, of the present application as filed and, in particular on pages 3-4, 6, 14-18, 20-21 (compound 6a) and throughout the examples. No new matter is believed to have been added.

With respect to claim amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

The Applicants thank the Examiner for removal of the "withdrawn" status for claim 28. For the record the Applicants note that claims 22, 25, and 28 were amended in the previous response to Office Action filed with the office on August 11, 2004, rather than claims 22, 24, and 28 as noted in the Office Action dated 11/01/2004. For the record, the Applicants also note that claims 53-59 and 62, which are currently withdrawn, appear to read on the elected group (Group 2) and species (polysorbate as surfactant, mannitol as bulking agent, elected echinocandin). Each of these claims ultimately depends from elected claim 22 which the Examiner agrees reads on the elected species. The additional limitations of claims 53-59 and 62 do not appear to the Applicant to exclude the elected species. While cancellation of claims 53, 56 and 59 renders this issue moot for those claims, the Applicants respectfully request that claims 54-55, 57-58 and 62 be considered and the status of "withdrawn" removed. The Applicants sincerely apologize for not having appreciated this issue at the time of filing the previous response.

The Applicants thank the Examiner for his indication of willingness to remove the “withdrawn” status for claim 31, which depends on elected claim 22, and its dependent claims 33-36 and request that he make this change of record. The Applicants note that each of the new claims (63-73) is directed to freeze-dried formulations and ultimately depends from claim 22 and therefore incorporates all of the limitations recited therein.

### **Request for Rejoinder**

The Applicants express their thanks to the Examiner for his responsiveness and note his indication of willingness to rejoin claims drawn to methods of making and using the elected formulations. Therefore, Applicants respectfully request rejoinder of withdrawn method claims 40-45 (directed to methods of making the claimed formulations) and 51-52 (directed to methods of using the claimed formulations) upon allowance of the elected product claims, in accordance with MPEP §821.04 (“Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. . . . However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.”). The Applicants also respectfully request that the Examiner remove the “withdrawn” status of formulation claim 46 which depends from claim 43 and incorporates all of the limitations of claim 22.

Independent method claims 40 and 43, and therefore their dependent claims 41-42 and 44-46, respectively, have been amended to incorporate all of the limitations of freeze-dried formulation claim 22. Method of treatment claim 51 as originally filed ultimately depends from product claim 22 pending in the instant application. Method of treatment claim 52 depends ultimately from claim 43. Applicants therefore respectfully request rejoinder of these method claims upon allowance of the product claim whose limitations they incorporate and further request that these method claims be examined for patentability in accordance with 37 C.F.R. §1.104 upon allowance of the product claims.

**Method of Treatment Claims**

With regard to the efficacy of the claimed echinocandin (compound 6(a)) as an antifungal, the Applicants draw the Examiner's attention to Groll *et al.*, (2001) *Antimicrobial Agents and Chemotherapy* **45**(10): 2845-2855, which is of record in the present application, having been submitted in the Supplemental Information Disclosure Statement dated January 14, 2004. The echinocandin compound recited in the pending claims (e.g., claim 22) corresponds to the compound referred to as "LY303366" or "Anidulafungin" in Groll *et al.* For convenience, the Applicants enclose here Appendix A (<http://www.doctorfungus.org/thedrugs/ly303366.htm>) which describes the various names of Anidulafungin as well as showing the corresponding structure.

Should the Examiner require additional information regarding the antifungal activity of compound 6(a) (also known as LY303366/anidulafungin), the Applicants will be happy to provide such upon request.

**Rejections under 35 U.S.C. §103**

While not acquiescing to the basic assertions put forth by the Examiner with respect to the rejections under 35 U.S.C. §103, in the interests of efficiently moving the prosecution of the present application forward, Applicants provide the comments appearing below.

A. Claims 22-27, 29, 30, 60, and 61 are rejected under 35 U.S.C. §103 as allegedly being unpatentable over Debono (USP 4,293,489) or Burkhardt (USP 5,965,525) or Burkhardt (USP 5,932,543) or Chen (USP 5,198,421) or Balkovec (USP 5,541,160) or Abbot (USP 4,304,716) in view of Andya (USP 6,267,958). The Applicants respectfully traverse this rejection.

As noted by the Examiner in the Office Action mailed 5/13/2004, the primary references do not teach a freeze-dried formulation that comprises an echinocandin, a micelle-forming surfactant and a bulking agent. The Applicants submit for the record that neither do any of the primary references cited by the Examiner teach or suggest the particular combination of the claimed echinocandin (compound 6(a)) with each of the components of the formulations as recited in the

claims as amended, and further, that Andya does not remedy this lack of teaching or suggestion. Additionally, it would be counter to the knowledge of those of skill in the art to pursue a freeze-dried formulation with the high levels of micelle-forming surfactant as required by the claims as it is known to formulation chemists that such high levels of surfactant have generally deleterious effects on the handling properties and stability of the resulting freeze dried product (*see* page 2, lines 1-21).

In view of the above remarks and amendments the Applicants respectfully request withdrawal of the rejection of claims 22-27, 29, 30, 60, and 61 under 35 U.S.C. §103.

**B.** Claims 22-27, 29, 30, 60, and 61 are rejected under 35 U.S.C. §103 as allegedly being unpatentable over Debono (USP 4,293,489) or Burkhardt (USP 5,965,525) or Burkhardt (USP 5,932,543) or Chen (USP 5,198,421) or Balkovec (USP 5,541,160) or Abbot (USP 4,304,716) in view of Horikoshi (USP 4,348,384). The Applicants respectfully traverse this rejection.

As noted by the Examiner in the Office Action mailed 5/13/2004, the primary references do not teach a freeze-dried formulation that comprises an echinocandin, a micelle-forming surfactant and a bulking agent. The Applicants submit that the primary references cited by the Examiner also do not teach or suggest the combination of the claimed echinocandin with the particular components of the formulations as recited in the amended claims, and further, that Horikoshi does not remedy this lack of teaching or suggestion.

In view of the above remarks and amendments the Applicants respectfully request withdrawal of the rejection of claims 22-27, 29, 30, 60, and 61 under 35 U.S.C. §103.

**C.** Claims 22-27, 29, 30, and 60 are rejected under 35 U.S.C. §103 as allegedly being unpatentable over Debono (USP 4,293,489) or Burkhardt (USP 5,965,525) or Burkhardt (USP 5,932,543) or Chen (USP 5,198,421) or Balkovec (USP 5,541,160) or Abbot (USP 4,304,716) in view of Staniforth (USP 6,153,224). The Applicants respectfully traverse this rejection.

As noted by the Examiner in the Office Action mailed 5/13/2004, the primary references do not teach a freeze-dried formulation that comprises an echinocandin, a micelle-forming

surfactant and a bulking agent. The Applicants submit that these primary references cited by the Examiner also do not teach or suggest the combination of the claimed echinocandin with the particular components of the formulations as recited in the amended claims, and further, that Staniforth does not remedy this lack of teaching or suggestion.

In view of the above remarks and amendments the Applicants respectfully request withdrawal of the rejection of claims 22-27, 29, 30, and 60 under 35 U.S.C. §103.

**D.** Claims 22-27, 29, 30, 60, and 61 are rejected under 35 U.S.C. §103 as allegedly being unpatentable over Debono (USP 4,293,489) or Burkhardt (USP 5,965,525) or Burkhardt (USP 5,932,543) or Chen (USP 5,198,421) or Balkovec (USP 5,541,160) or Abbot (USP 4,304,716) in view of Tarara (USP 6,565,885). The Applicants respectfully traverse this rejection.

As noted by the Examiner in the Office Action mailed 5/13/2004, the primary references do not teach a freeze-dried formulation that comprises an echinocandin, a micelle-forming surfactant and a bulking agent. The Applicants submit that these primary references cited by the Examiner also do not teach or suggest the combination of the claimed echinocandin with the particular components of the formulations as recited in the amended claims, and further, that Tarara does not remedy this lack of teaching or suggestion.

In view of the above remarks and amendments the Applicants respectfully request withdrawal of the rejection of claims 22-27, 29, 30, 60 and 61 under 35 U.S.C. §103.

**E.** Claims 22-27, 29, 30, 60, and 61 are rejected under 35 U.S.C. §103 as allegedly being unpatentable over Debono (USP 4,293,489) or Burkhardt (USP 5,965,525) or Burkhardt (USP 5,932,543) or Chen (USP 5,198,421) or Balkovec (USP 5,541,160) or Abbot (USP 4,304,716) in view of Backstrom (USP 5,952,008). The Applicants respectfully traverse this rejection.

As noted by the Examiner in the Office Action mailed 5/13/2004, the primary references do not teach a freeze-dried formulation that comprises an echinocandin, a micelle-forming surfactant and a bulking agent. The Applicants submit that these primary references cited by the

Examiner also do not teach or suggest the combination of the claimed echinocandin with the particular components of the formulations as recited in the amended claims, and further, that Backstrom does not remedy this lack of teaching or suggestion.

In view of the above remarks and amendments the Applicants respectfully request withdrawal of the rejection of claims 22-27, 29, 30, 60 and 61 under 35 U.S.C. §103.

**F.** Claims 22-27, 29, 30, 60, and 61 are rejected under 35 U.S.C. §103 as allegedly being unpatentable over Debono (USP 4,293,489) or Burkhardt (USP 5,965,525) or Burkhardt (USP 5,932,543) or Chen (USP 5,198,421) or Balkovec (USP 5,541,160) or Abbot (USP 4,304,716) in view of Bernstein (USP 6,689,390). The Applicants respectfully traverse this rejection.

As noted by the Examiner in the Office Action mailed 5/13/2004, the primary references do not teach a freeze-dried formulation that comprises an echinocandin, a micelle-forming surfactant and a bulking agent. The Applicants submit that these primary references cited by the Examiner also do not teach or suggest the combination of the claimed echinocandin with the particular components of the formulations as recited in the amended claims, and further, that Bernstein does not remedy this lack of teaching or suggestion.

In view of the above remarks and amendments the Applicants respectfully request withdrawal of the rejection of claims 22-27, 29, 30, 60 and 61 under 35 U.S.C. §103.

**G.** Claims 22-30, 60, and 61 are rejected under 35 U.S.C. §103 as allegedly being unpatentable over Debono (USP 4,293,489) or Burkhardt (USP 5,965,525) or Burkhardt (USP 5,932,543) or Chen (USP 5,198,421) or Balkovec (USP 5,541,160) or Abbot (USP 4,304,716) in view of Bouloumie (USP 6,284,277). The Applicants respectfully traverse this rejection.

As noted by the Examiner in the Office Action mailed 5/13/2004, the primary references do not teach a freeze-dried formulation that comprises an echinocandin, a micelle-forming surfactant and a bulking agent. The Applicants submit that these primary references cited by the Examiner also do not teach or suggest the combination of the claimed echinocandin with the

particular components of the formulations as recited in the amended claims, and further, that Bouloumie does not remedy this lack of teaching or suggestion.

In view of the above remarks and amendments the Applicants respectfully request withdrawal of the rejection of claims 22-30, 60 and 61 under 35 U.S.C. §103.

**H.** Claims 22-27, 29, 30, 60, and 61 are rejected under 35 U.S.C. §103 as allegedly being unpatentable over Debono (USP 4,293,489) or Burkhardt (USP 5,965,525) or Burkhardt (USP 5,932,543) or Chen (USP 5,198,421) or Balkovec (USP 5,541,160) or Abbot (USP 4,304,716) in view of Weers (USP 6,309,623). The Applicants respectfully traverse this rejection.

As noted by the Examiner in the Office Action mailed 5/13/2004, the primary references do not teach a freeze-dried formulation that comprises an echinocandin, a micelle-forming surfactant and a bulking agent. The Applicants submit that these primary references cited by the Examiner also do not teach or suggest the combination of the claimed echinocandin with the particular components of the formulations as recited in the amended claims, and further, that Weers does not remedy this lack of teaching or suggestion.

In view of the above remarks and amendments the Applicants respectfully request withdrawal of the rejection of claims 22-27, 29, 30, 60 and 61 under 35 U.S.C. §103.

**I.** Claims 22-27, 29, 30, and 60 are rejected under 35 U.S.C. §103 as allegedly being unpatentable over Debono (USP 4,293,489) or Burkhardt (USP 5,965,525) or Burkhardt (USP 5,932,543) or Chen (USP 5,198,421) or Balkovec (USP 5,541,160) or Abbot (USP 4,304,716) in view of Staniforth (USP 6,475,523). The Applicants respectfully traverse this rejection.

As noted by the Examiner in the Office Action mailed 5/13/2004, the primary references do not teach a freeze-dried formulation that comprises an echinocandin, a micelle-forming surfactant and a bulking agent. The Applicants submit that these primary references cited by the Examiner also do not teach or suggest the combination of the claimed echinocandin with the

particular components of the formulations as recited in the amended claims, and further, that Staniforth does not remedy this lack of teaching or suggestion.

In view of the above remarks and amendments the Applicants respectfully request withdrawal of the rejection of claims 22-27, 29, 30, and 60 under 35 U.S.C. §103.

**J.** Claims 22-27, 29, 30, 60, and 61 are rejected under 35 U.S.C. §103 as allegedly being unpatentable over Debono (USP 4,293,489) or Burkhardt (USP 5,965,525) or Burkhardt (USP 5,932,543) or Chen (USP 5,198,421) or Balkovec (USP 5,541,160) or Abbot (USP 4,304,716) in view of Dellamary (USP 6,433,040). The Applicants respectfully traverse this rejection.

As noted by the Examiner in the Office Action mailed 5/13/2004, the primary references do not teach a freeze-dried formulation that comprises an echinocandin, a micelle-forming surfactant and a bulking agent. The Applicants submit that these primary references cited by the Examiner also do not teach or suggest the combination of the claimed echinocandin with the particular components of the formulations as recited in the amended claims, and further, that Dellamary does not remedy this lack of teaching or suggestion.

In view of the above remarks and amendments the Applicants respectfully request withdrawal of the rejection of claims 22-27, 29, 30, 60 and 61 under 35 U.S.C. §103.

**K.** Claims 22-27, 29, 30, and 60 are rejected under 35 U.S.C. §103 as allegedly being unpatentable over Debono (USP 4,293,489) or Burkhardt (USP 5,965,525) or Burkhardt (USP 5,932,543) or Chen (USP 5,198,421) or Balkovec (USP 5,541,160) or Abbot (USP 4,304,716) in view of Edwards (USP 5,985,309). The Applicants respectfully traverse this rejection.

As noted by the Examiner in the Office Action mailed 5/13/2004, the primary references do not teach a freeze-dried formulation that comprises an echinocandin, a micelle-forming surfactant and a bulking agent. The Applicants submit that these primary references cited by the Examiner also do not teach or suggest the combination of the claimed echinocandin with the particular components of the formulations as recited in the amended claims, and further, that Edwards does not remedy this lack of teaching or suggestion.

In view of the above remarks and amendments the Applicants respectfully request withdrawal of the rejection of claims 22-27, 29, 30, and 60 under 35 U.S.C. §103.

## CONCLUSIONS

In view of the above, each of the presently pending composition claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the composition claims and to rejoin the withdrawn method claims upon allowance of the product claims and examine the rejoined claims in accordance with 37 C.F.R. §1.104. It is believed that the method claims requested to be rejoined are also in condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is earnestly invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **342312003601**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: January 31, 2005

Respectfully submitted,

By

  
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**APPENDIX A**

## BEST AVAILABLE COPY

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**Anidulafungin (LY303366)**[Manufacturer's webs](#)**Trade & Generic Names & General Features**

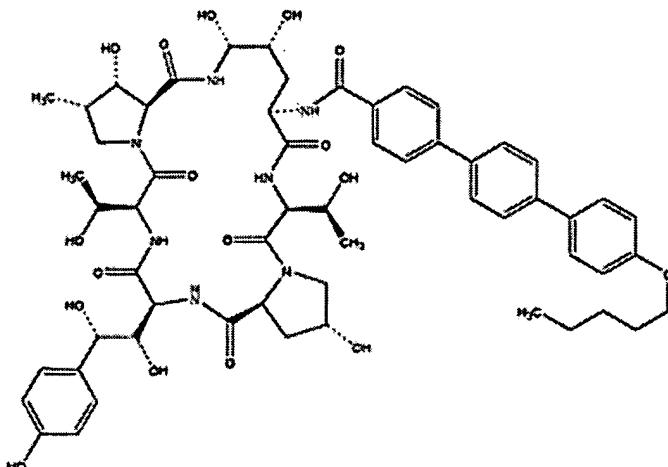
Anidulafungin (previously known as LY303366 and briefly also referred to as and V-echinocandin) is a glucan synthesis inhibitor of the echinocandin structure. It is composed of the echinocandin B nucleus with a terphenyl head group and a

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anidulafungin

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**Mechanism(s) of Action**

As with other echinocandins, anidulafungin blocks the synthesis of a major fungal wall component, 1-3-beta glucan, presumably via inhibition of 1,3-beta-glucanase [1156].

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## Susceptibility Patterns

Anidulafungin is active in vitro against *Candida* spp. However, anidulafungin *parapsilosis* and *C. guilliermondii* are relatively higher than those for the other. It has been shown to be fungicidal against some isolates of *C. albicans* and *C. krusei* [1628] [2088].

Anidulafungin does not have significant activity against *Cryptococcus neoformans*. Similarly, its activity against *Blastomyces dermatitidis*, *Sporothrix schenckii*, *Trichosporon beigelii*, *Acremonium strictum*, *Rhizopus arrhizus*, *Fusarium* spp., *Phialophora* spp. is limited. Anidulafungin MICs for *Histoplasma capsulatum*, *Cladophialophora bantiana*, *Pseudallescheria boydii*, and *Bipolaris* spp. are also relatively high [625] [2088].

As with *caspofungin*, activity of anidulafungin against *Aspergillus* spp. has been investigated by using a distinctive parameter, "minimum effective concentration" (MEC), as well as MIC [1158]. Anidulafungin MECs for *Aspergillus* are in an acceptable range and lower than the MICs [1626] [1519].

For anidulafungin MICs obtained for various types of fungi, see [susceptibility](#) and the [susceptibility database](#).

## **Usual Doses**

Typical doses for anidulafungin are not yet known.

## **Side-Effects**

Results of the clinical trials have not yet been reported.

## **Routes**

It has oral and intravenous formulations.

## **Current Status**

Anidulafungin is undergoing Phase II/III clinical trials.

## **References**

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